REMARKS

I. Amendments

A. Amendments to the Specification

The specification as been amended as shown above to provide International Publication references where appropriate.

B. Amendments to the Claims

Claims 1-19 were pending and examined. By amendment herein, claim 1 has been amended to make explicit that the modified plant zinc finger protein is non-naturally occurring and engineered, as described throughout the specification as filed, for example on page 11, lines 15-16; page 4, lines 15-16 and page 11, lines 17-20. Claim 12 has been amended to make explicit that the protein is encoded by the polynucleotide. Claim 17 has been amended to depend from claim 1. Thus, claims 1 to 19 are pending as shown above.

II. Restriction Requirement

Applicants note with appreciation that the restriction requirement has been withdrawn and all pending claims are under examination.

III. IDS

Applicants gratefully acknowledge receipt of the initialed and signed 1449 forms, filed with an IDS on December 30, 2002.

IV. 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1-19 stand rejected as allegedly not described in the specification as filed in such a way as to reasonably convey to the skilled artisan that applicants were in possession of the claimed subject matter. (Office Action, pages 2-4). In support of this rejection, the Office maintains that there are insufficient representative examples of the claimed modified plant ZFPs and nucleotides encoding these ZFPs. (Office Action, page 3).

Applicants traverse the rejection and supporting remarks.

The fundamental factual inquiry in written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Determining whether the written description requirement is satisfied is a question of fact and the burden is on the Examiner to provide evidence as to why a

skilled artisan would not have recognized that the applicant was in possession of claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976). It is not necessary that the application describe the claimed invention *in ipsis verba.* Rather, all that is required is that the specification reasonably convey possession of the invention. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). Finally, determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lange,* 209 USPQ 288 (CCPA 1981).

Furthermore, the Patent Office's own guidelines on written description are clear -- the written description requirement is highly fact-dependent and there is a strong presumption that an adequate written description of the claimed invention is present at the time of filing:

> [t]he description need only describe in detail that which is new or not conventional. This is equally true whether the claimed invention is a product or a process. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that the applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with known or disclosed correlation between function and structure, or some combination of such characteristics. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099, emphasis added).

Simply put, there is absolutely **no** requirement that Applicants exemplify (or reduce to practice) all sequences (amino acid or nucleotide) falling within the scope of the claims in order to adequately describe the claimed subject matter. Rather, the test is whether the specification, read in light of the state of the art, contains sufficient disclosure regarding the claimed molecules to satisfy the written description requirement. In the pending case, there is clearly a known (and disclosed) correlation between ZFP structure and binding function (*e.g.*, page 10, lines 6-9 of the specification). Furthermore, there is clear description in the specification of how to make the claimed ZFPs, using conventional molecular biology techniques. These facts, in combination with acknowledged description of an entire genus, establishes that the specification as filed more than adequately describes and details characteristics of the claimed molecules.

Claim construction

Because any written description inquiry must begin with claim construction, it is important to note at the outset of this discussion that the claims clearly recite both the structure (modified plant ZFP that is non-naturally occurring and engineered) and the function (binding to a target sequence) of the recited molecules. Therefore, when properly construed, it is plain that only proteins having the recited characteristics are encompassed by the pending claims. Furthermore, it is clear from the specification as filed that the written description requirement is met with respect the claimed molecules.

The specification describes the claimed molecules

As noted above, it is axiomatic that the specification need only describe in detail that which is new or not conventional. (See, Guidelines on Written Description, page 275). In the case at hand, a skilled artisan reading the specification would have known that Applicants were in possession of claimed molecules in view of the specification's extensive disclosure of (1) precise sequences falling in the scope of the claims (SEQ ID NOs:12-14, 17-19 and 35-98); (2) conventional, known methods of modifying amino acid and polynucleotide sequences (page 18, line 20 to page 21, line 15); and (3) the specification's description of, and the existence of conventional, known methods for, testing ZFPs for binding (*e.g.*, page 19, lines 29-30). In view of the disclosure of the specification and state of the art, it would have been plain to the skilled artisan that Applicants were in possession of the claimed subject matter at the time the specification was filed.

The Office acknowledges that the claimed genus is described

Turning now to the Office's assertion that there are insufficient representative examples described in the specification to adequately describe the claims, Applicants first note that a "representative number" does not mean that each and every species falling within the genus must be disclosed. (See, Guidelines on Written Description, reproduced in part above). Indeed, the Examiner acknowledges that the specification describes **an entire genus**. (Office Action, page 3, first full paragraph). Nonetheless, it was alleged that description of an entire genus was not representative of the scope of the original claims. In view of the foregoing amendments making explicit structural and functional features of the claimed molecules, Applicants submit that the genus admitted by the Office to be described by the specification as filed (including, for example, SEQ ID NOs:12-14, 17-19 and 35-98) is amply representative. Therefore, as

acknowledged by the Office, the written description requirement is satisfied with respect to the pending claims.

Furthermore, for the reasons noted above, it is well within the purview of the skilled artisan, in view of the teachings of the specification, to determine other embodiments falling within the scope of the claims. (See, *e.g.*, page 20, line 8 through page 21, line 13 and Examples). Accordingly, the representative number of embodiments (of an entire genus) disclosed in the specification more than adequately conveys to the skilled artisan that Applicants were in possession of the precisely claimed molecules at the time the application was filed.

There is ample description of the pending claims

The Office Action states that the claims are ". . . drawn to isolated polynucleotides encoding plant zinc finger proteins of undefined structure and unknown modification that bind to undefined target sequences of any size and any nature, including such isolated polynucleotides that further encode a domain of undefined structure and function that may repress or activate some unknown process." Applicants traverse these remarks, because the specification provides clear and ample description of the claimed subject matter.

First, the claimed modified plant zinc finger proteins do not have undefined structure. Multiple aspects of the structure of the zinc finger are disclosed in the specification: for example, tetrahedral coordination of a zinc atom by the conserved metal-binding amino acids cysteine and histidine, a conserved, 30-amino acid sequence, and the presence of a beta turn linked to an alpha helix. *See*, for example, page 1, line 17 through page 2, line 7 and page 17, lines 12-22. Furthermore, exemplary zinc finger sequences, and certain exemplary modifications of those zinc fingers, are provided in Example 1.

In addition to the aforementioned characteristics of zinc fingers (which were both disclosed in the specification and known in the art) and the explicit disclosure of exemplary zinc finger sequences, a description of zinc finger proteins is provided at page 16, line 26 through page 18, line 17.

Moreover, the term "modified plant zinc finger protein," as recited in the claims[1] is defined in the specification; therefore the statement that the claimed proteins contain "unknown modification" is incorrect.. *See*, for example, page 10, lines 17-24 and page 18, line 19 through page 21, line 15; in particular page 18, lines 20-24; page 19, lines 14-17 and page 20, lines 1-7.

[1] Applicants believe that the Office's focus on the word "modified" is misplaced, as it is a "modified plant zinc finger protein" that is recited in the claims; and this term must be considered in its entirety. To improperly focus on the meaning of the word "modified," taken out of its context in the claim, is akin to asserting lack of written description because the word "plant" or the word "finger" has not been explicitly defined in the specification.

Briefly, modification of plant zinc finger proteins can take one of several forms. For example, in contrast to naturally-occurring plant zinc finger proteins (in which the component zinc fingers are separated by large segments of amino acid sequence), the claimed modified plant zinc finger proteins comprise plant zinc fingers arranged in tandem arrays, *i.e.* with short segments of amino acid sequence, *e.g.*, 5-20 amino acids, intervening between individual zinc fingers (*see*, for example, page 18, line 30 through page 19, line 3). Modified plant zinc finger proteins can also contain alterations in the backbone amino acid sequence of a plant zinc finger as described, for example, at page 20, lines 13-22 and exemplified in Example 1 (pages 36-38).

The Office's assertion that the claimed proteins "bind to undefined target sequences of any size and nature" is also incorrect. The claimed subject matter relates to zinc finger proteins that can be engineered to bind to any target sequence of choice. *See*, for example, page 7, lines 3-5; page 8, lines 25-29; and page 20, lines 20-22. In support, the specification discloses methods for the engineering of zinc fingers to obtain a desired binding specificity. *See*, for example, page 2, line 20 through page 3, line 5; page 20, lines 23-28 and page 37, lines 10-20. The flexibility and wide applicability of the claimed compositions should not be used as a basis for asserting that they are incompletely described; and any requirement for Applicants to specify specific target sequences for the claimed proteins would prevent them from claiming what they believe to be their invention.

The Office's statement that the claimed polynucleotides "further encode a domain of undefined structure and function that may repress or activate some unknown process" is also untrue. Certain claims recite a "functional domain." Turning to the specification (page 15, lines 19-25) this term is clearly described as a protein or polypeptide sequence that has transcriptional modulation activity, or that is capable of interacting with proteins and/or protein domains that have transcriptional modulation activity. *See* also page 22, lines 20-29. Exemplary species of functional domains, such as activation and repression domains, are disclosed at page 22, line 30 through page 24, line 12.

Thus the specification, when properly considered, provides adequate written description for the claimed subject matter, and Applicants request that the rejection be withdrawn.[2]

The Case cited in the Office Action is not relevant

Furthermore, the Office's reliance on the *Regents of the Univ. Calif. v. Eli Lilly* is misplaced. The written description requirement of section 112 is highly fact dependent and the

[2] Applicants note that the Office's characterization of the exemplary modified plant ZFPs is also in error, at least to the extent that it characterizes them as containing a VP16 activation domain. They, in fact, contain a maize C1 activation domain. *See* page 40, lines 6-10 and Figure 1.

claims, disclosure and state of the art in *Eli Lilly* are entirely different from those in the case at hand. Indeed, the issue in *Eli Lilly* was not whether the specification disclosed a sufficient number of representative examples, but whether the specification disclosed any structure at all. In fact, the application at issue in *Eli Lilly* was completely devoid of any representative structural (sequence) examples. In contrast, Applicants' as-filed specification contains, and pending claims recite, specific structure and functional characteristics. Thus, because Applicants' disclosure and claims include both structure and physical properties, the case cited by the Office is not relevant to the pending claims.

For the reasons detailed above, it is clear that the specification describes the claimed molecules and, accordingly, withdrawal of this rejection is respectfully requested.

V. 35 U.S.C. 112, First Paragraph, Enablement

Claims 1-19 were rejected under 35 U.S.C. 112, first paragraph as allegedly not enabled by the specification as filed. (Office Action, pages 4 to 8). It is acknowledged that the specification enables isolated polynucleotides encoding the exemplified **genus** of modified plant zinc finger proteins. (Office Action, page 4, emphasis added). However, it is alleged that the specification does not enable sequences with undefined structure and unknown modifications that bind to an undefined target sequence. (Office Action, sentence bridging pages 4-5). It is also maintained that the specification does not enable the use of transcriptional functional domains other than VP16. (Office Action, pages 6-7). The Office Action further cites Segal et al. (2003) in support of the position that the functional domains are unpredictable. (See, Office Action, page 7).

Applicants traverse the rejection and supporting remarks.

Claim Construction

Because any enablement inquiry must begin with claim construction, it is important to reiterate at the outset of this discussion that the claims clearly recite both the structure and the function of the recited molecules. Thus, the claims do not, as asserted in the Office Action, recite "plant zinc finger proteins of undefined structure and unknown modification that bind to undefined target sequences of any size and any nature." (Office Action, sentence bridging pages 4-5). Rather, the claimed molecules are non-naturally-occurring proteins with modifications in the spacing and/or backbone sequence of a plant zinc finger protein, in which one or more of the zinc fingers are engineered, such that the claimed protein binds to a target site. Therefore, when

properly construed, it is plain that only sequences having the recited structure and function are encompassed by the pending claims.

Undue experimentation is not required to make and use the claimed molecules

When properly construed, it is clear that undue experimentation is not required to obtain the claimed compositions, because the claims are enabled throughout their scope and, in addition, because the reference cited by the Examiner does not in any way establish unpredictability.

The Examiner makes several arguments regarding enablement, including (1) the specification's disclosure of an entire genus somehow still failed to enable the claims as previously pending (Office Action, page 5); (2) the specification does not "explain how to alter the structure of the zinc finger backbone of non-canonical plant zinc finger proteins relative to any established non-canonical zinc finger standard or indicate the identity of such non-canonical zinc finger standards" (Office Action, page 6); and (3) the specification does not provide sufficient guidance of using functional domains other than VP16 (Office Action, pages 6-7). Applicants address each point in turn.

The specification fully enables modification of naturally occurring molecules

In the first and second points set forth above, the Examiner asserts that the specification is somehow deficient in explaining how to modify non-canonical zinc finger proteins, essentially on the basis that there are no working examples using non-canonical plant zinc finger proteins.

As a threshold matter, Applicants remind the Office that working examples are **never** required in order to establish enablement. Here, the specification provides ample details regarding the nature of "non-canonical" zinc finger proteins, as well as their design, selection and incorporation into modified plant zinc finger proteins as claimed. *See, e.g.,* page 7, lines 22-27; page 10, line 25 to page 11, line 7; and page 18, line 20 to page 21, line 15, particularly page 20, lines 15-22. As is well known to those working in the field, non-canonical zinc fingers can be readily produced by substituting one of the two conserved cysteine and/or one of the two conserved histidine residues of a canonical C_2H_2 ZFP.

Thus, the specification teaches precisely how one would go about identifying non-canonical plant zinc fingers, modifying these molecules and incorporating them into the claimed modified proteins. Indeed, the entire process is directly analogous to that set forth in the working examples of the specification with respect to canonical zinc fingers. Clearly, it would be routine to those of skill in the art in view of the teachings of the specification to align sequences,

design/select zinc fingers and incorporate the modified zinc fingers into a protein as claimed. Alternatively, it would be entirely routine for a skilled artisan to convert a canonical ZFP to a non-canonical ZFP, simply by replacing one or more of the conserved cysteine and/or histidine residues with another amino acid. As such, the evidence establishes that the specification enables the pending claims throughout their scope.

Furthermore, the pending claims are in no way directed to molecules having undefined structure or unknown modification. Indeed, the Office has itself acknowledged that the specification discloses an entire genus of molecules falling within the scope of the claims. (Office Action, page 5, first sentence of first full paragraphs). Applicants remind the Office that it is well settled that time-consuming or expensive experimentation is **not** undue if it is routine. (See, *e.g.,* PTO Training Manual on Enablement, pages 30-31, citing *United States v. Telectonics Inc.,* USPQ2d 1217, 1223 (Fed. Cir. 1988), *cert. denied* 490 U.S. 1046 (1989) holding the disclosure of a single exemplified embodiment and a method to determine other embodiments was enabling, even in the face of evidence that determining additional embodiments might require 6-12 months of effort and cost over $50,000). In the case at hand, the specification discloses an entire genus and methods of determining others, including those comprising non-canonical zinc fingers. The actual scope of the claims, and the nature of the guidance provided in the specification, along with the conventional nature of methods of modifying sequences and determining their function, all establish that the specification is fully enabling.

Therefore, Applicants note, to the extent this rejection is not obviated by the foregoing amendments, that the specification provides ample guidance on how to make and use the claimed molecules. Indeed, the fact that it would require only routine experimentation to determine other embodiments falling within the scope of the claims is equally applicable to the second and third points raised in the Office Action regarding non-canonical fingers and functional domains. In each and every instance, the claims encompass only those molecules that bind to a target sequence and exhibit the claimed structure. Accordingly, the claims are fully enabled by the specification as filed.

The specification fully enables molecules including functional domains

With particular regard to the Office's third point alleging that only VP16 functional domains are enabled by the specification, Applicants direct the Examiner's attention to pages 22, line 12 to page 26, line 3 of the specification, which contains extensive guidance on various functional domains. Moreover, Applicants note that the Office errs in asserting that only VP16 is exemplified -- all constructs tested in the Examples include the maize C1 activation domain.

Furthermore, it is utterly irrelevant that some functional domains may be more or less effective in certain cell types. Indeed, a functional domain may not even be necessary to achieve the desired result of modulation of gene expression. What is relevant is what the specification teaches in regards to such domains. Thus, the Examiner's citation of Segal *et al.* does not change the fact that any experimentation which might be needed to determine suitable functional domains is utterly routine in view of the teachings of the specification and the state of the art. Indeed, the cited passage from Segal is: (1) merely speculation unsupported by any experimentation on Segal's part and (2) restricted to what might function in *Arabidopsis*, rather what may or may not work in plants in general.

To summarize, the question of enablement is what the specification teaches one of skill in the art. In this case, the specification teaches one of skill in the art how to make and use the precisely claimed molecules. Indeed, Applicants have pointed to specific disclosures that establish enablement. Given the high level of skill in the art and routine nature of each step of the protein modification and screening procedures, it would not require undue experimentation to make and test modified plant ZFPs as of Applicants' filing date. Accordingly, the specification fully enables the pending claims and withdrawal of this rejection is respectfully requested.

VI. 35 U.S.C. 112, Second Paragraph

Claims 1, 12, 14, 15, 16 and 17 and claims dependent therefrom were rejected under 35 U.S.C. 112, second paragraph as allegedly indefinite. (Office Action, page 7-9).

It is axiomatic that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular disclosure at issue, (2) the teachings of the art, and (3) the interpretation that would be given by one possessing an ordinary level of skill in the pertinent art the time the invention was made. *See, e.g., In re Marosi,* 218 USPQ 289 (Fed. Cir. 1983). Consequently, a claim that is understandable to one of skill in the art meets the requirements of the second paragraph of 35 U.S.C. § 112.

To the extent that the foregoing amendments do not obviate these rejections, Applicants traverse on the grounds that the terms of the pending claims would have been clear to the skilled artisan in view of the specification as filed. The rejections are addressed in turn below.

A. Claims 1 and 17

Claims 1 and 17 were rejected as allegedly indefinite because the term "target sequence" was alleged to be unclear. (Office Action, page 8). Applicants traverse the rejection because the term is clearly and unambiguously defined, for example at page 16, lines 9-15.

B. Claim 12

Claim 12 was rejected as indefinite because it was alleged that there was insufficient antecedent basis for the recitation "amino acid residues." (Office Action, page 8). Claim 12 has been amended above as suggested by the Examiner to obviate this rejection.

C. Claim 14

Claim 14 was rejected as indefinite because the term "functional domain" was alleged to be unclear. (Office Action, page 8). Applicants note that the term is clearly defined, for example on page 15, lines 19-25. In addition, exemplary functional domains are disclosed at page 22, line 30 through page 24, line 12. Accordingly, the rejection is traversed.

D. Claim 15

Claim 15 was rejected as indefinite because the term "repressive domain" was alleged to be unclear. (Office Action, page 8). Again, the meaning of the term "repression domain," in its context as a species of functional domain, would readily be understood by the skilled artisan particularly in terms of Applicants' disclosure, for example on page 22, lines 23-27 ("modulation includes repression and activation of gene expression") and page 22, line 30 through page 23, line 18, particularly page 23, line 6 where it is stated that "another useful repression domain..." and line 10 where it is stated that "additional exemplary repression domains... ."

E. Claim 16

Claim 16 was rejected as indefinite because the term "activation domain" was alleged to be unclear. (Office Action, page 9). The term "activation domain" is definite in view of the teachings of the specification, for example on page 22, lines 23-27 where Applicants' teach that functional domains have the ability to modulate, including "repression and activation of gene expression" and page 23, line 19 through page 24, line 7, particular page 23, line 26 where Applicants note that "[a]dditional exemplary activation domains... ."

F. Claim 17

Claim 17 was rejected as indefinite because the metes and bounds of the term "modified" was alleged to be unclear. (Office Action, page 9).

Applicants submit that the term is clearly and repeatedly defined by Applicants through the specification. Indeed, as noted above, the term is be considered in context. In the pending

case, when properly viewed in context, the term "modified" is used with reference to naturally-occurring plant zinc finger proteins. *See, e.g.,* page 10, lines 17-24. Furthermore, additional structural characteristics of modified plant zinc finger proteins are provided, for example, at page 18, line 19 through page 21, line 15.

With respect to the alleged lack of clarity of certain words used by Applicants to describe a modified plant zinc finger protein, Applicants first note that further defining characteristics of modified plant zinc finger proteins, in addition to those in the cited passage from the specification, are provided, as set forth above. Moreover, Applicants respectfully remind the Office of the normal meaning of the words "variant" ("something that differs in form only slightly from something else") and "derived" ("received or obtained from a source").[3] Finally, the term "target sequence" has been defined in the specification, as noted above (Section VI.A of this Response). Accordingly, claim 17 is clear and definite as pending.

VII. 35 U.S.C. § 102

Claims 1-10 and 12-19 were rejected as allegedly anticipated by various references. (Office Action, pages 9-12).

A. Claims 1-4, 14 and 16-19 over Aoyama

Claims 1-4, 14 and 16-19 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Aoyama (1997) *Plant J.* 11:605-612 (hereinafter "Aoyama"). Aoyama is cited for allegedly teaching a tobacco plant host cell and transgenic tobacco plant comprising an isolated polynucleotide encoding a fusion of GAL4 and VP16. (Office Action, page 10).

The pending claims are directed to proteins comprising a zinc finger protein that is engineered to bind to a target sequence. *See,* for example, page 11, lines 3-16.

In contrast, the zinc finger protein portion of Aoyama's protein comprises a naturally-occurring, non-engineered yeast GAL4 zinc finger protein, thus failing to describe or suggest non-naturally occurring, engineered plant ZFPs, as claimed. Accordingly, Aoyama does not anticipate the pending claims and withdrawal of this rejection is respectfully requested.

B. Claims 1-9 and 12-19 over Takatsuji

Claims 1-9 and 12-19 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Takatsuji et al. (1996) *Biochemistry* 271(38):23368-23373 (hereinafter "Takatsuji"). Takatsuji is cited for allegedly teaching an isolated polynucleotide encoding a modified petunia plant zinc

[3] *See* attached pages from Webster's II New Collegiate Dictionary

finger protein comprising a tandem array of two canonical C_2H_2 zinc fingers. (Office Action, page 11).

The pending claims are directed to non-naturally-occurring, engineered, modified plant zinc finger proteins. Unlike the pending claims, Takatsuji relates entirely to naturally occurring, non-engineered EPF transcription factors. For these reasons, Takatsuji fails to recite each and every element of the claimed subject matter.

Furthermore, the binding characteristics of Takatsuji's EPF protein were tested against a variety of target sites, referred to as "probes." *See, e.g.,* Abstract and Figures. It is only these probes (target sequences) that Takatsuji alters to test whether the unmodified, naturally occurring, non-engineered EPF still binds. Thus, the mutations referred to in this reference are **not** modifications to the ZFP (or individual zinc fingers) but, rather, mutations in the target sequence.

Therefore, because Takatsuji fails to disclose or suggest modified plant zinc finger proteins as claimed, withdrawal of this rejection is respectfully requested.

C. Claims 1-8, 10 and 17 over Coupland

Claims 1-8, 10 and 17 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,077,994 (hereinafter "Coupland"). Coupland is cited for allegedly disclosing the *Arabidopsis* plant zinc finger protein CONSTANS. (Office Action, page 12).

Again, whereas the pending claims are directed to non-naturally occurring, engineered modified plant zinc finger proteins, Coupland discloses only the sequence of a naturally occurring, non-engineered plant ZFP. Col. 22 of Coupland does not, in fact, describe a modified plant zinc finger protein, but merely the fusion of sequences encoding a naturally-occurring, non-engineered ZFP to various promoter sequences. This is entirely unlike the claimed molecules, which include or encode non-naturally-occurring, engineered amino acid sequences.

In sum, there is not identity between the claimed molecules and the disclosures of Aaoyama, Takatsuji and/or Coupland and, accordingly, anticipation cannot be established. Therefore, withdrawal of the rejections based on 35 U.S.C. 102 is respectfully requested.

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CONCLUSION

Applicants submit that the claims are in condition for allowance and request early notification to that effect. If the Examiner has any further issues or wishes to discuss any of the foregoing, they are invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

Date: December 15, 2003

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